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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,208	03/08/2001	Wayne Parrott	UGA-855R	6703

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EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/802,208	PARROTT ET AL.	
	Examin r	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9, 14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-15 in Paper No. 15, submitted 13 January 2003, and Species D (transgenic plants) in Paper No. 18, submitted 21 February 2003, is acknowledged. Claims 16-18 are non-elected and withdrawn from consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 1, 2, and 13-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are broadly drawn towards any polynucleotide comprising at least one gene of interest and at least one selectable marker gene, wherein said marker gene comprises a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding SEQ ID NO: 3, 4, or 5, or functional fragments thereof; or a complement of said nucleotide sequence; and (b) a nucleotide sequence which selectively hybridizes under stringent conditions to a nucleotide sequence shown in SEQ ID NO: 1 or 2, or a complement thereof; or wherein said polynucleotide sequence is operably linked to a promoter; or any polynucleotide comprising a nucleotide sequence selected from the group consisting of (a) or (b) above, or wherein the polynucleotide comprises SEQ ID NO: 1 or 2.

The claims read on nucleotide sequences per se which can be found in nature and thus, are unpatentable to applicant. The polynucleotides, as claimed, have the same characteristics as those found naturally in the genome of cells, or as cellular precursors thereof, and therefore do not constitute patentable subject matter. See American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974), American Fruit Growers v. Brodgex Co., 283 U.S. 2 (1931), Funk Brothers Seed Co. v. Kalo Inoculant Co., 33 U.S. 127 (1948), Diamond v. Chakrabarty, 206 USPQ 193 (1980). It is suggested the term --isolated-- be inserted in line 1 of the claims before the term "polynucleotide", to identify a product that is not found in nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2: the recitation "wherein said polynucleotide is operably linked to a promoter" renders the claims indefinite. The polynucleotide comprises a gene of interest and a selectable marker gene. It is not clear if the promoter is intended to direct transcription of a single mRNA that comprises the transcript of both the gene of interest and the marker gene, or if it is intended for a promoter to be operably linked to each of the nucleotides sequences of the gene of interest and the selectable marker gene.

In claim 3: the recitation "Transgenic cells transformed with a gene of interest and the polynucleotide molecule of claim 1" renders the claim indefinite. The polynucleotide molecule of claim 1 comprises a gene of interest. It is then not clear if the gene of interest mention in line 1 of claim 3 is meant to be the same as, or different from, the gene of interest present in the polynucleotide molecule.

In claim 7: the recitation "derivative" renders the claim indefinite. It is not exactly clear what compounds are encompassed by the recitation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any polynucleotide comprising at least one gene of interest and at least one selectable marker gene, wherein said marker gene comprises a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding SEQ ID NO: 3, 4, or 5, or functional fragments thereof; or a complement of said nucleotide sequence; and (b) a nucleotide sequence which selectively hybridizes under stringent conditions

to a nucleotide sequence shown in SEQ ID NO: 1 or 2, or a complement thereof; or wherein said polynucleotide sequence is operably linked to a promoter; transgenic plant cells transformed with any gene of interest and said polynucleotide, wherein the selectable marker gene gives said cells a selective advantage in the presence of a marker compound; or wherein said marker compound is arabitol, ribitol, mannitol, or a derivative thereof; a plant or plant tissue regenerated from said cells; a method of selecting transformed plant cells from a population of cells, comprising introducing into the genome of a cell a gene of interest and a selectable marker gene, supplying to the population a marker compound wherein transformed cells have a selective advantage over non-transformed cells due to expression of the gene of interest or the selectable marker gene in the presence of the compound, wherein the marker gene comprises a nucleotide sequence selected from (a) or (b) above and said compound comprises arabitol, mannitol, ribitol, or a derivative thereof; transformed plant cells selected according to said method; plant or plant tissue regenerated from said cells, or seed produced from said plant; or any polynucleotide comprising a nucleotide sequence selected from the group consisting of (a) or (b) above.

The specification indicates that SEQ ID NO: 1 sets forth the nucleotide sequence of the arabitol dehydrogenase gene from *Escherichia coli* strain C, and that SEQ ID NO: 2 sets forth the nucleotide sequences of ribitol dehydrogenase, ribitol kinase, and ribitol transporter, from the ribitol operon of *E. coli* strain C. SEQ ID NOs: 3-5 set forth the amino acid sequences of the ribitol dehydrogenase, ribitol kinase, and ribitol transporter, respectively (paragraph bridging pages 4-5).

However, the specification does not describe any functional fragments of nucleotide sequences encoding SEQ ID NOs: 3-5. The structural features of SEQ ID NOs: 3-5 that are

essential to their functional activities are not described. Differences in their structures then cannot be correlated with their functions. The specification also does not describe nucleotide sequences that selectively hybridize under stringent conditions to SEQ ID NO: 1 or 2. The recitation "stringent conditions" does not provide any indication of the level of stringency of the hybridization, and the claims therefore broadly encompass hybridization under any condition. It is well accepted in the art that hybridizations that occur under low and moderate stringency conditions will allow the hybridization of unrelated sequences to the template sequence. Further, the claims do not indicate the function of the hybridizing nucleotide sequence, and therefore encompass sequences that are functionally unrelated to SEQ ID NOs: 1 and 2. The functions of such sequences are not described in the specification. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states: "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA... Accordingly, the specification does not provide a written description of the invention..." Also see Fiers 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". The specification also does not describe any derivatives of arabitol, mannitol, or ribitol. Other structures that have their function are not described or even suggested in the specification. Given the breadth of the claims encompassing nucleotide sequences encoding fragments of SEQ ID

NOs: 3-5, all nucleotide sequences that hybridize to SEQ ID NOs: 1 and 2 under all stringency conditions, and derivatives of arabitol, mannitol, and ribitol, and lack of guidance as discussed above, the specification fails to provide an adequate written description of the multitude of nucleotide sequences and marker compounds encompassed by the claims.

5. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards any polynucleotide comprising at least one gene of interest and at least one selectable marker gene, wherein said marker gene comprises a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding SEQ ID NO: 3, 4, or 5, or functional fragments thereof; or a complement of said nucleotide sequence; and (b) a nucleotide sequence which selectively hybridizes under stringent conditions to a nucleotide sequence shown in SEQ ID NO: 1 or 2, or a complement thereof; or wherein said polynucleotide sequence is operably linked to a promoter; transgenic plant cells transformed with any gene of interest and said polynucleotide, wherein the selectable marker gene gives said cells a selective advantage in the presence of a marker compound; or wherein said marker compound is arabitol, ribitol, mannitol, or a derivative thereof; a plant or plant tissue regenerated from said cells; a method of selecting transformed plant cells from a population of cells, comprising introducing into the genome of a cell a gene of interest and a selectable marker gene, supplying to the population a marker compound wherein transformed cells have a selective advantage over

non-transformed cells due to expression of the gene of interest or the selectable marker gene in the presence of the compound, wherein the marker gene comprises a nucleotide sequence selected from (a) or (b) above and said compound comprises arabitol, mannitol, ribitol, or a derivative thereof; transformed plant cells selected according to said method; plant or plant tissue regenerated from said cells, or seed produced from said plant; or any polynucleotide comprising a nucleotide sequence selected from the group consisting of (a) or (b) above.

As discussed above, the specification indicates that SEQ ID NO: 1 sets forth the nucleotide sequence of the arabitol dehydrogenase gene from *Escherichia coli* strain C, and that SEQ ID NO: 2 sets forth the nucleotide sequences of ribitol dehydrogenase, ribitol kinase, and ribitol transporter, from the ribitol operon of *E. coli* strain C. SEQ ID NOs: 3-5 set forth the amino acid sequences of the ribitol dehydrogenase, ribitol kinase, and ribitol transporter, respectively (paragraph bridging pages 4-5). The specification also provides a prophetic example for using SEQ ID NO: 1, SEQ ID NO: 2, or nucleotide sequences encoding SEQ ID NOs: 3-5 in a method for transforming plant cells, in which the expressed arabitol dehydrogenase, or ribitol dehydrogenase, kinase, and transporter, provide a selective advantage to transformed cells, which allow for the selection of transformed versus non-transformed cells. The method involves treating a population of putatively transformed plant cells with arabitol, ribitol, or mannitol. The cells expressing SEQ ID NOs: 1, 2, or 3-5 supposedly have a selective advantage over non-transformed cells in the presence of arabitol, ribitol, or mannitol (Examples 3-4, pages 23-24).

However, the specification does not teach any nucleotide sequences encoding functional fragments of SEQ ID NOs: 3-5. The specification does not teach how the structure of SEQ ID

NOs: 3-5 may be changed without affecting their functional activities. No teaching is provided as to what amino acid sequences may be deleted without affecting protein activity. In the absence of further guidance teaching what residues may be changed in SEQ ID NOs: 3-5 without affecting their activities, undue experimentation would be required by one skilled in the art to produce nucleotide sequences of fragments of SEQ ID NOs: 3-5 and test them for retention of functional activity. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 UPSQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence). The specification also does not teach any nucleotide sequences that hybridize to SEQ ID NOs: 1 or 2 under all stringency conditions. The claims broadly encompass all levels of hybridization stringencies, which would allow the binding of unrelated nucleotide sequences. The specification does not teach how one skilled in the art is to use unrelated sequences with the claimed method. Further, the specification does not provide any guidance at all in how one skilled in the art would make or find the claimed derivatives of arabitol, ribitol, or mannitol. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Further, the specification does not teach that the claimed method provided for positive selection of transformed plant cells. As discussed above, the specification provides only prophetic direction, and does not teach that transformed plant cells were actually produced, and

that selective advantage was conferred over non-transformed cells, allowing for their positive selection. The teachings of the specification assume that the claimed selective marker genes will be functionally active in plant cells. However, it is premature to conclude that the product of all transgenes will be active when expressed in transgenic plants. Sung et al. (Plant Cell Physiol., 1997, Vol. 38, pages 484-489), for example, teach transgenic plants transformed with a MADS box gene, AGL2, wherein the transgenic plants were not phenotypically different from non-transgenic plants (page 488). The specification also does not teach how the transformed plants should be selected- that is, the nature of the selective advantage of the transformed cells versus the non-transformed cells is not taught. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine the type of selective advantage that is conferred to the transformed plant tissue, so that one may distinguish the transformed plant tissue from the non-transformed tissues. See Genentech, Inc. V. Novo Nordisk, A/S, *supra*. Furtherstill, the claims indicate that the nucleotide sequence introduced into the plant cells may be those encoding SEQ ID NOs: 3, 4, or 5, which indicates that the claimed method can work with only one of these nucleotide sequences. However, all three products are required to metabolize ribitol. The specification does not demonstrate that cells expressing only ribitol transporter, for example, can metabolize or grow in medium comprising ribitol. Furthermore, the claimed method also indicates that transformed cells only expressing the gene of interest can have the selective advantage (step (c) of claim 7, "due to expression or transcription of the gene of interest or the selectable marker gene", emphasis added). It is not clear, and not taught by the specification, how a random gene of interest that is unrelated to the marker compound can confer a selective advantage to transformed plant cells in the presence of

the marker compound. Even further, the claims indicate that the selectable marker may be the complement of the nucleotide sequence of parts (a) and (b) or claims 1 and 7. It is not at all clear how these complements can be used in the claimed invention, when they do not encode arabitol dehydrogenase, ribitol dehydrogenase, ribitol kinase, and ribitol transporter. See Genentech, Inc. V. Novo Nordisk, A/S, *supra*. Given the breadth of the claims, unpredictability of the art, and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3, 5, 6, and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Bojsen et al. (U.S. Patent No. 5,767,378).

The claims are broadly drawn towards any polynucleotide comprising at least one gene of interest and at least one selectable marker gene, wherein said marker gene comprises a

nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding SEQ ID NO: 3, 4, or 5, or functional fragments thereof; or a complement of said nucleotide sequence; and (b) a nucleotide sequence which selectively hybridizes under stringent conditions to a nucleotide sequence shown in SEQ ID NO: 1 or 2, or a complement thereof; or wherein said polynucleotide sequence is operably linked to a promoter; or transgenic cells transformed with a gene of interest and said polynucleotide.

Bojsen et al. teach polynucleotide molecules comprising a gene of interest and a nucleotide sequence encoding an enzyme involved in mannose metabolism, operably linked to a promoter, and transgenic plant cells and plants comprising said polynucleotide (col. 6, line 35 to col. 14, line 5; claims). The property of hybridizing to instant SEQ ID NO: 1 or 2 under a stringent hybridization condition is inherent to the nucleotide sequence encoding an enzyme involved in mannose metabolism taught by Bojsen et al. The method of producing the transformed plant cells and plants taught by Bojsen et al. differ from method of production of the cells and plants of instant claims 10 and 11. However, the process of making the claimed cells and plants does not distinguish the cells and plants themselves from those taught by the reference. See In re Thorpe, 227 USPQ 964,966 (Fed. Cir. 1985), which teaches that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process, if the process of making the product fails to distinguish the two products. The transgenic cells and plants of Bojsen et al. and instant claims 10 and 11 both comprise nucleotide sequences that can hybridize to instant SEQ ID NO: 1 or 2 under a stringent hybridization condition. It would be obvious to collect seed from the transformed plants of

Bojsen et al., for the purpose of propagation. Thus, the claimed invention was clearly prima facie obvious as a whole to one of ordinary skill in the art, if not anticipated by Bojsen et al.

7. Claims 1-15 are rejected. Claims 16-18 are non-elected and withdrawn from consideration.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

May 15, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER